COMPUTATION OF WALL THICKNESS

Related Applications

This application is based on two prior copending provisional applications, Serial No. 60/456,680, filed on March 20, 2003, and Serial No. 60/456,912, filed on March 21, 2003, the benefit of the filing dates of which is hereby claimed under 35 U.S.C. § 119(e).

Field of the Invention

The present invention generally relates to imaging vascular vessels, and more specifically, to determining a wall thickness of a vascular vessel from an image of the vascular vessel.

Background of the Invention

According to the National Center for Health Statistics, cardiovascular disease is the leading cause of death in the United States. Carotid atherosclerosis is one of the main causes of stroke. Atherosclerosis is a form of arteriosclerosis characterized by the deposition of atheromatous plaques containing cholesterol and lipids on the innermost layer of the walls of large- and medium-sized arteries. Improved methods of diagnosis, treatment, and prevention of these diseases would result in a significant improvement in the quality of life of patients and a concomitant decrease in health care costs.

Traditionally, the degree to which lumen stenosis has occurred is used as a morphological marker for high risk (i.e., vulnerable) plaques. Clinical, X-ray, computerized tomography (CT), ultrasound, and magnetic resonance (MR) angiography are used to determine lumen stenosis. The determination of lumen stenosis lacks a unified approach, as evidenced by the two different methods of stenosis quantification that are most often used – the North American Symptomatic

Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial. Regardless of the method used, it has been demonstrated that lumen narrowing is a poor indicator of patient vulnerability to strokes. In symptomatic patients, evidence of lumen narrowing predicted only about one out of four strokes. In asymptomatic patients, evidence of lumen narrowing predicted only about one out of ten strokes. Clearly, it would be desirable to employ a more accurate predictor of a patient's risk of having a stroke using conventional imaging procedures.

Some studies indicate the importance of plaque morphological factors (in addition to stenosis) in determining thromboembolic risk. Specifically, ultrasonographic studies show that plaque thickness is a better predictor of transient ischemic attacks than vessel stenosis. Unfortunately, ultrasound measurement of plaque thickness is not highly reproducible, since such measurements produce results varying from 13.8% to 22.4%. Further evidence of the importance of plaque morphology was documented in a study by NASCET investigators showing increasing risk for stroke with ulcerated plaques, as compared to non-ulcerated plaques with similar degrees of stenosis. These results suggest that a comprehensive, quantitative analysis of plaque morphology, including lumen stenosis, wall thickness, and ulceration, will better identify vulnerable plaques.

Recent studies have shown that Magnetic Resonance Imaging (MRI) is capable of identifying plaque constituents and measuring plaque morphology. MR plaque imaging may therefore be a useful technique for characterizing plaque morphology and tissue constituents in one examination, thereby assessing both aspects of vulnerable plaque. However, current MRI techniques fail to provide the data necessary for comprehensive, quantitative analysis of plaque morphology. It would be desirable to develop methods of using MRI to obtain accurate tracing of lumen and wall boundaries, a reasonable definition of carotid wall thickness, accurate computation of lumen surface roughness, and a reasonable definition of plaque burden indexes. Techniques for tracing lumen and wall boundaries and computing lumen surface roughness have been suggested. However, a consistent and reliable technique for estimating lumen wall thickness from an image of a lumen has not been taught in the prior art.

In addition to wall thickness, other quantitative morphological parameters can be defined to assess plaque morphology. Morphological description refers to the methods that produce numeric morphological descriptors and is carried out subsequent to morphological representation. A morphological description method generates a morphological descriptor vector (also called a feature vector) from a given shape. The goal of morphological description is to uniquely characterize a shape using its morphological descriptor vector.

Previous work has established the reproducibility of in-vivo measurements of area and volume from a carotid artery MR image. These studies indicate a good agreement between in-vivo and ex-vivo measurements. Specifically, volume measurements matched to within 4%-6% and cross-sectional area measurements matched to within 5%-11% for two independent MR scans performed within 2 weeks that were reviewed by two independent reviewers. In addition, it has been determined that different contrast weighted images (T1, T2, and proton density) of comparable image quality will yield similar results in lumen and vessel wall area measurements. Such results indicate that morphological descriptors extracted from MRI may be used to characterize vascular shape variance. However, the prior art does not define a specific set of useful morphological descriptors. It would be desirable to provide vascular morphological descriptors that are based on lumen boundary, wall boundary, and wall thickness, and to use such descriptors to evaluate plaque morphology.

Summary of the Invention

A first aspect of the present invention is directed to a method for determining vessel wall thickness from an image of a vessel. The method is implemented automatically with a computing device. In the method, an imaging system is coupled to the computing device and is configured to perform the wall thickness determination. The method automatically estimates vessel wall thickness at any point along the perimeter of either luminal or vessel outer wall boundaries. Both Delaunay triangulation and multiresolution tiling. Multiresolution tiling is used to determine a MaxMin angle lemma. As defined in the Delaunay triangulation, the MaxMin angle property relates a minimal energy function to triangulation angles. Thus, the

determination of the MaxMin angle lemma enables the minimum energy function to calculate wall thickness. In the method, it is assumed that a single boundary cannot overlap itself.

A second aspect of the present invention is directed to a set of vascular shape descriptors that are based in part on wall thickness, which can be used to evaluate plaque morphology. 32 vascular morphological descriptors are defined as a function of lumen boundary, wall boundary, and wall thickness. The morphological descriptors include area descriptors, lumen boundary descriptors, wall boundary descriptors, wall thickness descriptors, complexity lumen-wall descriptors, and complexity thick-wall descriptors. The area descriptors define lumen area, wall area, and a ratio of wall area to lumen area. The lumen boundary descriptors, wall boundary descriptors, and wall thickness descriptors demonstrate shape variance, while the complexity lumen-wall descriptors and complexity thick-wall descriptors demonstrate relative variance. The descriptors can be used to automate the clinical plaque analysis.

Brief Description of the Drawing Figures

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same becomes better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 schematically illustrates edge flipping, used with Delaunay triangulation in the present invention for determining the thickness of a lumen wall from an image of the lumen;

FIGURES 2A-2E schematically illustrate multiresolution tiling, which is used in the present invention;

FIGURE 3 is a visual representation of a wall thickness estimation in accord with the present invention, as applied to carotid phantom MR images;

FIGURE 4 are exemplary patient carotid MR images;

FIGURE 5 is a visual representation of wall thickness estimation, as applied to the patient carotid MR images of FIGURE 4, in accord with the present invention;

FIGURE 6 schematically illustrates the outer wall boundary and the lumen boundary, which with the wall thickness value, are employed to define a plurality of morphological descriptors used to evaluate plaque morphology, in accord with a second aspect of the present invention;

FIGURE 7A schematically illustrates stenosis of a lumen, wherein the lumen and wall areas change without a change in the lumen shape;

FIGURE 7B schematically illustrates stenosis of a lumen, wherein the lumen boundary changes shape, but the outer wall boundary does not;

FIGURE 7C schematically illustrates a lumen, wherein the lumen boundary does not change changes shape, but the outer wall boundary does;

FIGURE 7D schematically illustrates stenosis of a lumen, wherein there is variance in the lumen boundary and the outer wall boundary;

FIGURE 8A are exemplary images of a patient's carotid artery obtained at three different facilities, showing extracted contours;

FIGURE 8B are exemplary images of a patient's carotid artery obtained at three different facilities, showing minimum and maximum wall thicknesses;

FIGURE 9A are exemplary images of different patients' carotid arteries, illustrating extracted contours;

FIGURE 9B are exemplary images of different patients' carotid arteries, again showing minimum and maximum wall thicknesses; and

FIGURE 10 is a block diagram of a computer system suitable for implementing the present invention.

Description of the Preferred Embodiment

The present invention is directed to calculating the wall thickness of a lumen from an image of the lumen. In this invention, a set of 32 vascular shape descriptors, which are based in part on wall thickness, can be used to evaluate plaque morphology. The method of calculating wall thickness and the set of vascular descriptors can be combined to enable automated clinical plaque analysis to be achieved.

The method for estimating wall thickness employs both Delaunay triangulation and multiresolution tiling. In a particularly preferred

implementation, the lumen is a blood vessel, and the wall thickness of the blood vessel determined by the method can be used as a predictor of whether the patient is at risk of a stroke.

Delaunay triangulation is widely used for unstructured mesh generation in computer graphics and is suitable for many applications. The present invention utilizes one of the Delaunay triangulation properties, the MaxMin angle property, to define a minimum energy function, which is then used to calculate wall thickness. Using Delaunay triangulation enables consistent and stable results to be achieved. Multiresolution tiling is then employed to determine the MaxMin angle.

The MaxMin Angle Lemma is as follows. *Among all triangulations of a finite set* $s \subseteq \Re^2$, *the Delaunay triangulation maximizes the minimum angle.* This Lemma implies that the smallest angle in any triangulation is no larger than the smallest angle in the Delaunay triangulation.

An elementary operation of Delaunay triangulation is edge flipping. An edge flip substitutes two new triangles for two old triangles, but does not decrease the smallest angle in the triangles. Edge flipping can be used to change angles, as is shown in FIGURE 1. In FIGURE 1, edge *ab* is flipped to edge *cd*. The old angles are α_1, β_1, $\gamma_1+\gamma_2$, α_2, β_2, and $\theta_1+\theta_2$, and the new angles achieved by edge flipping are γ_1, θ_1, $\beta_1+\beta_2$, γ_2, θ_2, and $\alpha_1+\alpha_2$. A minimal energy function to compute thickness based on maximizing the minimum angle in a set of triangulations $s \subseteq \Re^2$ is defined as follows:

$$Min\left(\frac{1}{\sum_{i=1}^{N}\theta_i}\right) \tag{0}$$

where θ_1 is the minimum angle in a triangle i, and N is the number of triangulations in $s \subseteq \Re^2$. Thus, thickness can be calculated by minimizing the energy function (i.e., using Equation 0, above).

A key aspect of the present invention is to use tiling optimization to determine the smallest angle in a triangulation. Tiling optimization is described

below, in connection with FIGURE 2A-2E. Tiling optimization involves inserting new vertices and edges from the lower resolution level. Referring to FIGURE 2E, vertex *d* is inserted into triangle *abc* in the lower resolution level, yielding quadrilateral *abcd*. The inserted edge *bd* splits quadrilateral *abcd* into triangles *abd* and *dbc*. In FIGURE 2E, new vertices are indicated by circles, and inserted edges are indicated by dashed lines. Note triangles *abd* and *dbc* match the curve of the lumen more closely than triangle *abc* does, thus inserting the vertex *d* and edge *bd* increases the resolution.

Now assume line *ab* is a "suspect" edge. Line *ab* belongs to two triangles, *abc* and *abd*. The union of those two triangles is a convex quadrangle, *abcd*. Thus, *ab* and *cd* can be flipped. Formally, this means that line *ab*, triangle *abc* and triangle *abd* are removed from the triangulation and new line *cd*, new triangle *acd* and new triangle *bcd* are added to the triangulation (FIGURE 1 shows such a flipping operation). Schematically, the result of edge flipping resembles a tetrahedron with the front and back superimposed. Such edge flipping is an elementary operation to convert an arbitrary triangulation to the Delaunay triangulation. In the present invention, a stack is used to maintain an invariant, so that unless an edge is locally Delaunay, it resides on the stack. Initially, all "suspect" edges are pushed on the stack, and the following operation is performed for each edge:

```
WHILE stack is non-empty DO
    POP ab from stack and unlabel it;
    IF ab not locally Delaunay then flip ab to cd;
        FOR xy ∈ {ac, bd} do
            IF xy unlabeled then
                label xy and push it on stack
            END IF
        ENDFOR
    END IF
END WHILE
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Multiresolution analysis enables the tiling problem to be optimized. A first step is to reduce the size of the problem by using multiresolution analysis to find low-resolution approximations to the original contours. Detail is then added to the low-resolution tiling by inserting edges at newly added vertices, and improving the tiling by local edge flipping under the control of the minimal energy function. The specific steps involved in multiresolution tiling are as follows:

1. Decompose each contour into a set of low-resolution versions based on wavelet analysis as disclosed by M. David, "Multiresolution Tiling," *Computer Graphics Form*, vol. 13, no. 5, pp. 325-340, 1994. FIGURE 2A schematically illustrates a contour 202 and a contour 204. In the context of a vascular vessel, contour 202 corresponds to a lumen boundary, while contour 204 corresponds to an outer wall boundary. FIGURE 2B schematically illustrates contour 202 and contour 204 being decomposed into a low resolution set of individual points 206.

2. Compute tiling for the low-resolution contours using the "greedy" method described by S. Ganapathy and T. Dennehy in "A new triangulation method for planar contours," *Computer Graphics*, vol. 16, pp. 69-75, 1982. FIGURE 2C schematically illustrates the triangulation of points 206 in each low resolution set.

3. Label all cross edges as "suspect" edges and put them into a stack. Edges *ab* and *bc* are cross edges, in that such edges couple points on each contour (see FIGURE 2C).

4. Optimize the tiling by flipping the local edge under control of the minimal energy function.

5. Insert a new vertex on both contours at triangle edge of the tiling from the lower resolution level, so that the former triangles are now quadrilaterals. FIGURE 2D schematically illustrates the insertion of additional vertices, such as vertex *d*. Triangle *abc* is now quadrilateral *abcd*.

6. Construct an edge from the inserted vertex to the quadrilateral vertex on the other contour, splitting the quadrilateral into two triangles, as shown in FIGURE 2E (see edge *bd*). .

7. Label each old cross edge as a "suspect" edge and put them into a stack.

8. Optimize the tiling by flipping the local edge under control of the minimal energy function.

9. Repeat steps 5 - 9 until the original resolution (or a desired resolution) is reached.

To validate the performance of the thickness estimation, two experiments were designed. A first experiment estimated the thickness of carotid phantom MR images (image size=256 x 256; pixel size=10.32 mm; slice thickness=2.0 mm; number of slices=6). A second experiment applied the thickness estimation to carotid MR images (image size=256 x 256; pixel size=10.25 mm; slice thickness=2.0 mm; number of slices=30) of a patient. The phantom MR images were used to test the consistency of thickness method. The patient's carotid MR images were used to show that the thickness can readily characterize different vascular morphological types.

FIGURE 3 is a visual representation of results obtained in the first experiment, where wall thicknesses of carotid phantom MR images were estimated. Portions a1-a6 of FIGURE 3 correspond to original images with extracted contours, whereas portions b1-b6 correspond to estimated thickness. The bright lines in portions b1-b6 indicate the maximum and minimum thicknesses. Table 1 summarizes a few of the morphological indexes calculated from thicknesses estimated on the phantom images of FIGURE 3. The morphological indexes include thickness mean, thickness standard deviation, minimum thickness, maximum thickness, ratio of minimum thickness to maximum thickness (Min/Max), and the ratio of thickness standard deviation to thickness mean (Dev/Mean). Because the morphology should not change much in a short segment of common artery of the carotid phantom, the standard deviation of mean thickness, minimum thickness, and maximum thickness should be very

small. Table 1 shows that the ratio of the standard deviation to each of the average of mean thickness, the average of minimum thickness, and the average of maximum thickness is 0.55%, 1.54%, and 0.85%, respectively. These results indicate that the thickness measurement method of the present invention is stable and consistent.

Table 1 Morphological indexes calculated on the phantom images (mm)

Image No	Mean	Deviation	Min Thick	Max Thick	Min/Max	Dev/Mean
1	4.142	0.098	3.874	4.394	0.882	0.024
2	4.119	0.111	3.788	4.339	0.873	0.027
3	4.134	0.091	3.945	4.393	0.898	0.022
4	4.148	0.085	3.935	4.380	0.898	0.020
5	4.183	0.100	3.941	4.452	0.885	0.024
6	4.166	0.081	3.895	4.368	0.892	0.019
Average	4.149	0.094	3.896	4.388	0.888	0.023
Deviation	0.023	0.011	0.060	0.037	0.010	0.003
Dev/Average	0.55%		1.54%	0.85%	1.12%	

FIGURES 4 and 5 are provided to illustrate the results obtained in the second experiment, where wall thicknesses of a patient's carotid MR images were estimated. For example, image a14 shows the bifurcation of the common carotid artery. FIGURE 4 includes original images, with extracted contours, while FIGURE 5 indicates the estimated thicknesses with bright lines corresponding to maximum and minimum thicknesses.

Table 2 summarizes a few of morphological indexes calculated from thicknesses based on patient's images in FIGURE 5, which include thickness mean, thickness standard deviation, minimum thickness, maximum thickness, ratio of minimum thickness to maximum thickness (Min/Max), and ratio of thickness standard deviation to thickness mean (Dev/Mean).

Table 2 Morphological indexes calculated on patient images in FIGURE 5

Image	Bifurcation	Mean	Deviation	MinThick	MaxThick	Min/Max	Dev/Mean
1	-13	0.91	0.12	0.73	1.18	0.62	0.13
2	-12	0.85	0.10	0.61	1.12	0.55	0.12
3	-11	0.88	0.08	0.69	1.09	0.64	0.09
4	-10	0.83	0.07	0.65	1.01	0.64	0.08
5	-9	0.93	0.15	0.60	1.23	0.49	0.16
6	-8	0.84	0.12	0.51	1.09	0.47	0.14
7	-7	1.07	0.24	0.67	1.67	0.40	0.23
8	-6	0.98	0.17	0.66	1.27	0.52	0.18
9	-5	1.25	0.41	0.76	2.13	0.36	0.33
10	-4	1.17	0.40	0.64	2.10	0.30	0.34
11	-3	1.94	0.94	0.69	3.91	0.18	0.48
12	-2	1.72	0.83	0.74	3.57	0.21	0.48
13	-1	2.49	1.14	1.04	4.65	0.22	0.46
14	0	2.72	1.64	0.57	5.69	0.10	0.60
15	1	3.98	1.67	1.11	6.19	0.18	0.42
16	2	3.79	1.56	1.20	5.99	0.20	0.41
17	3	3.71	1.37	1.54	5.83	0.26	0.37
18	4	3.62	1.29	1.67	5.64	0.30	0.36
19	5	2.58	1.64	0.60	5.65	0.11	0.64
20	6	2.62	1.57	0.79	5.28	0.15	0.60
21	7	2.60	1.58	0.98	5.48	0.18	0.61
22	8	2.57	1.58	0.66	5.31	0.12	0.62
23	9	2.37	1.39	0.85	5.06	0.17	0.59
24	10	2.22	1.30	0.75	4.53	0.17	0.59
25	11	1.82	0.94	0.92	3.57	0.26	0.52
26	12	2.03	0.83	0.92	3.50	0.26	0.41
27	13	1.21	0.35	0.62	2.00	0.31	0.29
28	14	0.97	0.26	0.54	1.53	0.35	0.27
29	15	0.87	0.20	0.39	1.19	0.33	0.22
30	16	0.93	0.19	0.54	1.28	0.42	0.20

Table 2 shows that different wall shapes can be readily separated into different categories based on morphological indexes. For example, if Min/Max is employed as an index to separate the portions shown in FIGURE 5 into different categories, and the threshold for Min/Max is set to 0.3, images a1-a9 fall in a first group, images a10-a26 fall in a second group, and images a27-a30 fall into a third group.

As noted above, the present invention is also includes a set of 32 vascular morphological descriptors, which are defined based on measurements of lumen

boundary, wall boundary, and wall thickness. Techniques for boundary tracing are known in the art (see Han, C. et al. 2001. "A fast minimal path active contour model." *IEEE Transactions on Image Processing*, 10(6):865-873, the disclosure and Figures of which are hereby specifically incorporated herein by reference). Determination of wall thickness based on using Delaunay triangulation and multiresolution tiling is discussed in detail above. The morphological description includes area descriptors, simple descriptors, and complexity descriptors.

The area descriptors show lumen area, wall area, and their relative position and ratio. The simple descriptors include lumen boundary descriptors, wall boundary descriptors, and wall thickness descriptors. The complexity descriptors include complexity lumen-wall descriptors, and complexity thick-wall descriptors. The simple descriptors demonstrate shape variance, while the complexity descriptors demonstrate relative variance between lumen boundary, outer boundary, and wall thickness. The reproducibility of the descriptors has been tested on MR images obtained from both normal and diseased human carotid arteries.

The formulation for the morphological descriptors will first be discussed, followed by specific definitions of the descriptors for vascular morphological analysis. Finally, empirical data supporting the present invention will be discussed.

FIGURE 6 schematically illustrates an outer wall boundary 104 and a lumen boundary 102 that are used in connection with the wall thickness value to define the morphological descriptors. A maximum radii 108 and a minimum radii 106 can then be computed, as discussed in detail below.

In regard to the formulation of the morphological descriptors of the present invention, suppose that a contour has N vertices and the edges connect the vertices in the following order: $[(x_1, y_1), (x_2, y_2), \cdots, (x_N, y_N)]$, with the last vertex being connected to the first vertex. The area of a contour is defined as:

$$Area = abs\left(\frac{1}{2}\sum_{i=1}^{N} x_i y_{i\oplus 1} - x_{i\oplus 1} y_i\right) * p_x * p_y \qquad (1)$$

where $i \oplus 1$ is $(i+1) \bmod N$, and p_x, p_y are the edge size of rectangular pixel.

A radius of a contour is defined as a distance from the centroid to a point on the contour. The centroid of a contour is defined as:

$$Centroid(x,y) = \{Centroid(x), Centroid(y)\} = \left\{ \frac{1}{N}\sum_{i=1}^{N} x_i,\ \frac{1}{N}\sum_{i=1}^{N} y_i \right\} \tag{2}$$

A radius i of a contour is defined as:

$$Radius(i) = sqrt\left((x_i - Centroid(x))^2 * p_x^{\,2} + (y_i - Centroid(y))^2 * p_y^{\,2}\right) \tag{3}$$

The minimum radii and the maximum radii of a contour are defined as:

$$MinRadii = \frac{1}{2\delta}\sum_{i=l_{\min}-\delta}^{l_{\min}+\delta} Radius(i) \tag{4}$$

$$MaxRadii = \frac{1}{2\delta}\sum_{i=l_{\max}-\delta}^{l_{\max}+\delta} Radius(i) \tag{5}$$

where δ is a neighborhood 100 around a minimum radius location $l_{\min}$, and the maximum radius location $l_{\max}$, as shown in FIGURE 6:

$$l_{\min} = \arg\min_{i=1,2,\cdots N}(Radius(i)) \tag{6}$$

$$l_{\max} = \arg\max_{i=1,2,\cdots N}(Radius(i)) \tag{7}$$

The mean and standard deviation of the radii of a contour are defined as:

$$MeanRadii = \frac{1}{N}\sum_{i=1}^{N} Radius(i) \tag{8}$$

$$SDRadii = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(Radius(i) - MeanRadii)^2} \tag{9}$$

Similarly, suppose that wall thicknesses of number M are being evaluated. The minimum of all wall thicknesses, the maximum of all wall thicknesses, the

mean of all wall thicknesses, and standard deviation of all wall thicknesses are defined as:

$$MinThick = \frac{1}{2\delta} \sum_{j=l_{\min}-\delta}^{l_{\min}+\delta} Thickness(i) \tag{10}$$

$$MaxThick = \frac{1}{2\delta} \sum_{j=l_{\max}-\delta}^{l_{\max}+\delta} Thickness(i) \tag{11}$$

$$MeanThick = \frac{1}{M} \sum_{i=1}^{M} Thickness(i) \tag{12}$$

$$SDThick = \sqrt{\frac{1}{N} \sum_{i=1}^{M} (Thickness(i) - MeanThick)^2} \tag{13}$$

where δ is the neighborhood around the minimum thickness location, $l_{\min}$, and maximum thickness location, $l_{\max}$, defined as:

$$l_{\min} = \arg\min_{i=1,2,\cdots,M} (Thickness(i)) \tag{14}$$

$$l_{\max} = \arg\max_{i=1,2,\cdots,M} (Thickness(i)) \tag{15}$$

The specific definitions of the area descriptors, the simple descriptors, and the complexity descriptors of the present invention will now be provided. Area descriptors include lumen area (*LumenArea*), outer-wall boundary area (*OuterArea*), wall area (*WallArea*), and the ratio of the lumen area to the outer-wall boundary area (*LORatio*). The lumen area and outer-wall boundary area are calculated from Equation (1). The wall area and the ratio are computed from:

$$WallArea = OuterArea - LumenArea \tag{16}$$

$$LORatio = (LumenArea/OuterArea) * 100\% \tag{17}$$

The *LumenArea*, *OuterArea*, and *WallArea* specify the physical area size of the artery, and the *LORatio* indicate the *LumenArea* as a percentage of *OuterArea*. These area descriptors represent the stenosis and variation along a

vessel, as schematically shown in FIGURES 7A-7D. In FIGURE 7A the lumen and wall areas change without shape variance.

The simple descriptors are based on one dimensional distance, e.g., one of lumen radii, outer-wall boundary radii, and wall thickness. The simple descriptors include lumen boundary descriptors, outer-wall boundary descriptors, and wall thickness descriptors. Each simple descriptor group includes the mean, the minimum, the maximum, the ratio of the minimum to the maximum, the ratio of minimum to the mean, the ratio of the mean to the maximum, and the ratio of the standard deviation to the mean of a feature parameter. The mean descriptor, the minimum descriptor, and the maximum descriptor demonstrate the physical radii size or thickness size, and the ratio descriptors show the relationship among the mean descriptor, the minimum descriptor, and the maximum descriptor. The lumen boundary descriptors, wall boundary descriptors, and wall thickness descriptors indicate shape variance.

FIGURE 7B schematically illustrates lumen boundary shape variance without outer wall boundary variance. FIGURE 7C schematically illustrates outer wall boundary shape variance without lumen area variance. FIGURE 7D schematically illustrates lumen boundary and outer wall boundary variance. Thus, it will be evident that the descriptors provide detail relating to vessel morphology.

The mean of the lumen boundary radii (*MeanLRadii*), the minimum of the lumen boundary radii (*MinLRadii*), and the maximum of the lumen boundary radii (*MaxLRadii*) are computed from Equations (4), (5), and (8), respectively. The ratio of the minimum of the lumen boundary radii to the maximum of the lumen boundary radii (*LMMDev*), the ratio of the minimum of the lumen boundary radii to the mean of the lumen boundary radii (*LMinDev*), the ratio of the mean of the lumen boundary radii to the maximum of the lumen boundary radii (*LMaxDev*), and the ratio of the standard deviation of the lumen boundary radii to the mean of the lumen boundary radii (*LMeanDev*) are calculated from:

$$LMMDev = (1.0 - MinLRadii / MaxLRadii) * 100\% \quad (18)$$

$$LMinDev = (1.0 - MinLRadii / MeanLRadii) * 100\% \quad (19)$$

$$LMaxDev = (1.0 - MeanLRadii / MaxLRadii) * 100\% \quad (20)$$

$$LMeanDev = (SDLRadii / MeanLRadii) * 100\% \quad (21)$$

The mean of the outer-wall boundary radii (*MeanWRadii*), the minimum of the outer-wall boundary radii (*MinWRadii*), and the maximum of the outer-wall boundary radii (*MaxWRadii*) are computed using Equations (4), (5), and (8), respectively. The ratio of the minimum of the outer-wall boundary radii to the maximum of the outer-wall boundary radii (*WMMDev*), the ratio of the minimum of the outer-wall boundary radii to the mean of the outer-wall boundary radii (*WMinDev*), the ratio of the mean of the outer-wall boundary radii to the maximum of the outer-wall boundary radii (*WMaxDev*), and the ratio of the standard deviation of the outer-wall boundary radii to the mean of the outer-wall boundary radii (*WMeanDev*) are calculated as follows:

$$WMMDev = (1.0 - MinWRadii / MaxWRadii) * 100\% \quad (22)$$

$$WMinDev = (1.0 - MinWRadii / MeanWRadii) * 100\% \quad (23)$$

$$WMaxDev = (1.0 - MeanWRadii / MaxWRadii) * 100\% \quad (24)$$

$$WMeanDev = (SDWRadii / MeanWRadii) * 100\% \quad (25)$$

The mean of all wall thicknesses (*MeanThick*), the minimum of all wall thicknesses (*MinThick*), and the maximum of all wall thicknesses (*MaxThick*) are computed using Equations (10), (11), and (12), respectively. The ratio of the minimum of all wall thickness to the maximum of all wall thicknesses (*TMMDev*), the ratio of the minimum of all wall thicknesses to the mean of all wall thicknesses (*TMinDev*), the ratio of the mean of all wall thickness radii to the maximum of all wall thicknesses (*TMaxDev*), and the ratio of the standard deviation of all wall thicknesses to the mean of all wall thicknesses (*TMeanDev*) are determined as follows:

$$TMMDev = (1.0 - MinThick / MaxThick) * 100\% \quad (26)$$

$$TMinDev = (1.0 - MinThick / MeanThick) * 100\% \quad (27)$$

$$TMaxDev = (1.0 - MeanThick / MaxThick) * 100\% \quad (28)$$

$$TMeanDev = (SDThick / MeanThick) * 100\% \quad (29)$$

The complexity descriptors characterize the relationship between two dimensional distances, i.e., lumen radii to outer boundary radii, or wall thickness to outer boundary radii. The complexity descriptors include lumen-wall descriptors, and thick-wall descriptors, which show relative variance between lumen boundary shape to outer wall boundary shape, and wall thickness shape to wall boundary shape. As noted above, FIGURES 7A-&D schematically illustrate such variances.

Complexity lumen-wall descriptors include the ratio of the minimum of the lumen radii to the mean of all wall radii (*MinLW*), the ratio of the maximum of the lumen radii to the mean of all wall radii (*MaxLW*), the ratio of the mean of the lumen radii to the mean of all wall radii (*MeanLW*), and the ratio of the distance between the lumen centroid and the outer-wall boundary centroid to the mean of all wall radii (*EccentricityW*). The *EccentricityW* demonstrates the level of relative variance of the eccentric distance between the lumen boundary and the outer-wall boundary to the mean of wall radii. *MinLW, MaxLW, MeanLW* and *EccentricityW* are determined as follows:

$$MinLW = (MinLRadii / MeanWRadii) * 100\% \quad (30)$$

$$MaxLW = (MaxLRadii / MeanWRadii) * 100\% \quad (31)$$

$$MeanLW = (MeanLRadii / MeanWRadii) * 100\% \quad (32)$$

$$EccentricityW = (Dist / MeanWRadii) * 100\% \quad (33)$$

where

$$Dist = sqrt\left((x_W - x_L)^2 * p_x^{\,2} + (y_W - y_L)^2 * p_y^{\,2}\right) \quad (34)$$

and (x_L, y_L), (x_W, y_W) are respectively the lumen centroid and the outer-wall boundary centroid, and p_x, p_y are the pixel size.

Complexity Thick-wall descriptors include the ratio of the minimum of all wall thicknesses to the mean of all wall radii (*MinTW*), the ratio of the maximum of all wall thicknesses to the mean of all wall radii (*MaxTW*), and the ratio of the mean of all wall thicknesses to the mean of all wall radii (*MeanTW*), calculated as follows:

$$MinTW = (MinThick / MeanWRadii) * 100\% \quad (35)$$

$$MaxTW = (MaxThick / MeanWRadii) * 100\% \quad (36)$$

$$MeanTW = (MeanThick / MeanWRadii) * 100\% \quad (37)$$

To assess the reproducibility of the morphological descriptors described above, two experiments were designed to apply the morphological descriptors to data obtained from images of a carotid artery. In a first experiment, a volunteer traveled to three different facilities (the University of Washington Medical Center, the University of Utah Medical Center, and the Mayo Clinic), and the volunteer's carotid artery was scanned with a flow suppressed fast spin sequence at each facility. While each facility employed different imaging software, the scanners employed at each facility were identical, and the same imaging parameters were employed at each facility (image size=512 x 512/pixel size=0.32 mm/slice thickness=2.0 mm/number of slices=9). The resulting image data from each facility were reviewed by one expert. In a second experiment, two independent MR scans were taken within two weeks for each of fifteen patients distributed across two different facilities (the University of Washington Medical center and the Veteran's Affairs Puget Sound Health Care System). Each of the two MR scans for the same patient were performed by the same facility. Each facility employed the same imaging parameters (image size=512 x 512 pixels, pixel size=0.25 mm, slice thickness=2.0 mm, and number of slices=10). The fifteen patients ranged in age from 42 to 69 years. All protocols and consent forms were approved by each facilities' review board. In each patient, at least one side of the carotid stenosis was over 50% and less than 80%, as determined by duplex ultrasound examination. Two scans of fifteen patients ought to have yielded thirty

carotid artery images for analysis; however, locational mismatching and poor image quality (caused by patient movement during scanning) resulted in only 24 useful carotid artery images being available for analysis. Two radiologists independently traced each patient's lumen and outer-wall boundaries using the semi-automatic Snake algorithm. Using the lumen and outer wall boundaries thus obtained, and wall thicknesses obtained as described above (i.e., using a combination of Delaunay triangulation and multiresolution tiling), the value of each of the 32 morphological descriptors noted above were automatically calculated. The bifurcation of the carotid artery was used as a reference point to match the carotid physical location so that the reproducibility of the results could be determined.

The reproducibility of the morphological descriptors were evaluated using pooled relative standard deviation (PRSD). The PRSD for a sample is calculated as follows:

$$PRSD = \sqrt{\frac{\sum_{p=1}^{l}\sum_{j=1}^{m} RSD_{p,j}^{2}}{l \bullet m}} \cdot 100\% \tag{38}$$

where

$$RSD_{p,j} = \frac{\sqrt{\sum_{i=1}^{n}\left(x_{p,j,i} - \bar{x}_{p,j}\right)^{2}}}{\bar{x}_{p,j}} \tag{39a}$$

or

$$RSD_{p,j} = \sqrt{\frac{\sum_{i=1}^{n}\left(x_{p,j,i} - \bar{x}_{p,j}\right)^{2}}{n-1}} \tag{39b}$$

$$\bar{x}_{p,j} = \frac{1}{n}\sum_{i=1}^{n} x_{p,j,i}$$

where $x_{p,j,i}$ is a morphological descriptor, $i = 1, 2, \cdots, n$ is the index of a sample, $j = 1, 2, \cdots, m$ is the slice index of carotid artery, and $p = 1, 2, \cdots, l$ is the index of patient's carotid arteries. For the three sites experiment, $i = 1, 2, 3$, $j = 1, 2, \cdots, 9$, and $p = 1$. For this experiment, $i = 1, 2$, $j = 1, 2, \cdots, 10$, and $p = 1, 2, \cdots, 24$. Equation (39a) is used for descriptors that have a physical dimension, e.g., *LumenArea*, *OuterArea*. Equation (39b) is used for dimensionless descriptor, e.g., *LORatio, LMMRadii*. Equation (39b) expresses the standard deviation as a percentage of the maximum of the possible range of ratios, which is 1.0.

FIGURES 8A and 8B are visual representations of images obtained in the first experiment, where the carotid artery of one patient was imaged at three different facilities, and the images were reviewed by the same expert. FIGURES 8A and 8B show wall thickness in three slices around the bifurcation of the patient's left carotid artery. Images M-a1, M-a2, and M-a3 of FIGURES 8A and 8B were obtained at the Mayo Clinic, Images U-a1, U-a2, and U-a3 of FIGURES 8A and 8B were obtained at the University of Utah Medical Center, and Images W-a1, W-a2, and W-a3 of FIGURES 8A and 8B were obtained at the University of Washington Medical Center. In FIGURE 8A, each image includes extracted contours, while in FIGURE 8B, each image includes maximum and minimum thicknesses. Table 3 shows the pooled relative PRSD of the morphological descriptors of the patient's left carotid artery. The maximum PRSD among the descriptors is less than 7%. The results of this site-to-site study suggest that the morphological descriptors can be used to evaluate MR images obtained from different sites.

Table 3 PRSD of the descriptors: 1 volunteer imaged at 3 different facilities.

Descriptors	PRSD	Mean	Descriptors	PRSD	Mean
lumenArea	3.71%	30.84	WMinDev	2.05%	0.11
OutArea	3.28%	61.30	WMaxDev	1.73%	0.08
LORatio	1.87%	0.50	Mean Thick	5.53%	1.27
WallArea	6.06%	30.46	Min Thick	6.26%	0.84
MeanLRadii	1.93%	3.11	Max Thick	6.17%	1.80
MinLRadii	2.77%	2.67	TMMThick	3.00%	0.53
MaxLRadii	3.25%	3.46	TDMDev	2.95%	0.19
LMMRadii	3.07%	0.20	TMinDev	2.13%	0.34
LDMDev	1.16%	0.07	TMaxDev	3.93%	0.29
LMinDev	2.31%	0.13	MinLW	1.79%	0.61
LMaxDev	1.63%	0.09	MaxLW	2.29%	0.78
MeanWRadii	1.58%	4.40	MeanLW	1.37%	0.70
MinWRadii	2.82%	3.89	MinTW	1.06%	0.19
MaxWRadii	2.32%	4.85	MaxTW	2.39%	0.41
WMMRadii	2.74%	0.18	MeanTW	1.38%	0.29
WDMDev	1.04%	0.06	Ecc	1.30%	0.05

FIGURES 9A and 9B are visual representations of images obtained in the first experiment, where the carotid arteries of 15 patients were imaged two different times over a two week period at the same facility, and the images were reviewed by different experts. FIGURES 9A and 9B do not show each image; instead, selected images from the experiment are provided. In FIGURE 9A, each image includes extracted contours, while in FIGURE 9B, each image includes an indication of maximum and minimum wall thicknesses. Table 4 shows the PRSD of the fifteen patients. The maximum PRSD among the descriptors is less than 12%. In Tables 3 and 4, descriptors involving outer wall measurements, such as wall area, tend to be less precise (expressing a relatively large PRSD), due to the greater difficulty in tracing outer wall boundaries. Ratios such as LORatio (lumen

area/outer wall area) tend to be more precise (indicating a relatively smaller PRSD), because the ratios are in general small in magnitude, and therefore, the PRSD is small. The results of Tables 3 and 4 suggest that the morphological descriptors of the present invention can be used to monitor vascular plaque morphology progression and regression based on patient MR images.

Table 4 PRSD of the descriptors of fifteen patients (different analysts).

Descriptors	PRSD	Mean	Descriptors	PRSD	Mean
LumenArea	6.44%	36.67	WMinDev	2.65%	0.12
OutArea	5.85%	85.75	WMaxDev	2.32%	0.10
LORatio	3.02%	0.42	Mean Thick	8.68%	1.82
WallArea	10.19%	49.09	Min Thick	11.55%	0.98
MeanLRadii	3.23%	3.32	Max Thick	11.18%	2.90
MinLRadii	4.93%	2.79	TMMThick	5.26%	0.63
MaxLRadii	4.34%	3.83	TDMDev	4.26%	0.27
LMMRadii	3.85%	0.26	TMinDev	5.58%	0.44
LDMDev	1.43%	0.09	TMaxDev	4.68%	0.35
LMinDev	3.08%	0.16	MinLW	2.74%	0.54
LMaxDev	2.27%	0.12	MaxLW	3.32%	0.73
MeanWRadii	2.87%	5.17	MeanLW	2.40%	0.64
MinWRadii	3.77%	4.49	MinTW	2.06%	0.19
MaxWRadii	4.32%	5.81	MaxTW	5.87%	0.56
WMMRadii	3.87%	0.21	MeanTW	2.42%	0.36
WDMDev	1.40%	0.07	Ecc	3.46%	0.11

Descriptor Legend

1. *LumenArea*: The area of the lumen.
2. *OuterArea*: The area of the outer-wall boundary.
3. *WallArea*: The area of the wall between the lumen boundary and the outer wall boundary.
4. *LORatio*: The ratio of the lumen area to the outer-wall boundary area.

5. *MeanLRadii*: The mean of the lumen boundary radii.
6. *MinLRadii*: The minimum of the lumen boundary radii.
7. *MaxLRadii*: The maximum of the lumen boundary radii.
8. *LMMDev*: The ratio of the minimum of the lumen boundary radii to the maximum of the lumen boundary radii.
9. *LMinDev*: The ratio of the minimum of the lumen boundary radii to the mean of the lumen boundary radii.
10. *LMaxDev*: The ratio of the mean of the lumen boundary radii to the maximum of the lumen boundary radii.
11. *LMeanDev*: The ratio of the standard deviation of the lumen boundary radii to the mean of the lumen boundary radii.
12. *MeanWRadii*: The mean of the outer-wall boundary radii.
13. *MinWRadii*: The minimum of the outer-wall boundary radii.
14. *MaxWRadii*: The maximum of the outer-wall boundary radii.
15. *WMMDev*: The ratio of the minimum of the outer-wall boundary radii to the maximum of the outer-wall boundary radii.
16. *WMinDev*: The ratio of the minimum of the outer-wall boundary radii to the mean of the outer-wall boundary radii.
17. *WMaxDev*: The ratio of the mean of the outer-wall boundary radii to the maximum of the outer-wall boundary radii.
18. *WMeanDev*: The ratio of the standard deviation of the outer-wall boundary radii to the mean of the outer-wall boundary radii.
19. *MeanThick*: The mean of all wall thicknesses.
20. *MinThick*: The minimum of all wall thicknesses.
21. *MaxThick*: The maximum of all wall thicknesses.
22. *TMMDev*: The ratio of the minimum of all wall thicknesses to the maximum of all wall thicknesses.
23. *TMinDev*: the ratio of the minimum of all wall thicknesses to the mean of all wall thickness.
24. *TMaxDev*: The ratio of the mean of all wall thicknesses to the maximum of all wall thicknesses.

25. *TMeanDev*: The ratio of the standard deviation of all wall thicknesses to the mean of all wall thicknesses.
26. *MinLW*: The ratio of the minimum of the lumen radii to the mean of all wall radii.
27. *MaxLW*: The ratio of the maximum of the lumen radii to the mean of all wall radii.
28. *MeanLW*: The ratio of the mean of the lumen radii to the mean of all wall radii.
29. *EccentricityW*: The ratio of the distance between the lumen centroid and the outer-wall boundary centroid to the mean of all wall radii.
30. *MinTW*: The ratio of the minimum of all wall thicknesses to the mean of all wall radii.
31. *MaxTW*: The ratio of the maximum of all wall thicknesses to the mean of all wall radii.
32. *MeanTW*: The ratio of the mean of all wall thicknesses to the mean of all wall radii.

The set of vascular morphological descriptors discussed above can be used to analyze vascular morphology. While the use of all of the descriptors defined above is preferred, it should be understood that the present invention is not limited to the use of the full set of descriptors defined above, as fewer than the thirty two descriptors defined above can be used to analyze plaque morphology. Preferably, at least two descriptors will be employed. The descriptors are defined based on lumen boundary, outer-wall boundary, and wall thickness. Prior art techniques are employed to define the lumen boundary and outer-wall boundary (i.e., the extracted contours of FIGURES 8A and 9A). Wall thickness is calculated using Delaunay triangulation and multiresolution tiling, as discussed above. The set of vascular morphological descriptors are calculated using the lumen boundary, the outer-wall boundary, and wall thickness values. The descriptors quantify the morphological size of the lumen, the outer-wall, and wall thickness, as well as their relative variant relationship. Empirical testing indicates the maximum PRSD among the descriptors is less than 7%. The descriptors show high reproducibility,

with descriptors involving outer wall measurements showing the greatest variation.

In a preferred implementation, wall thickness calculations and the set of vascular morphological descriptors are automatically generated using a computing device. Such a computing device can be included in an imaging system used to collect the images, or the computing device can process stored images that are separately collected, perhaps at a previous time. The computing device can be configured to provide visual results, such as illustrated in the examples of FIGURES 8B and 9B, where minimum and maximum wall thicknesses are represented visually (the bright lines). The computing device can also be configured to provide numerical data relating to wall thicknesses, as well as the PRSD data provided in the examples shown in Tables 3 and 4. The computing device can be further configured to use the set of vascular morphological descriptors for clinical plaque analysis, producing results that quantitatively predict risk factors based on plaque morphology.

System for Implementing the Present Invention

FIGURE 10 and the following related discussion are intended to provide a brief, general description of a suitable computing environment for practicing the present invention. As indicated above, the method of estimating wall thickness and the morphological descriptors can be used to automate analysis of plaque morphology. Thus one aspect of the present invention is an automated system to generate lumen image data (particularly image data corresponding to vascular structures) and to evaluate such image data. The processing can be implemented on a personal computer or other computing device. Those skilled in the art will appreciate that the present invention may be practiced with other computing devices, including a laptop and other portable computers, multiprocessor systems, networked computers, mainframe computers, and on other types of computing devices that include a processor, a memory, and optionally, a display.

The system of FIGURE 10 includes a generally conventional imaging apparatus 30 (preferably an MRI system) that is controlled by a computer 32. Computer 32 may be a generally conventional personal computer (PC) or a

dedicated controller specifically intended for controlling imaging apparatus 30. Although not specifically shown, when imaging apparatus 30 is implemented using an MRI system, imaging apparatus 30 will include a magnet to create a permanent magnetic field, a plurality of gradient coils to produce spatial variations of magnetic field, and an RF transceiver and receiver systems to transmit and receive RF signals to and from a plurality of RF coils, in the manner well known to those of ordinary skill in the art of MRI. Accordingly, details of the MRI apparatus, or other well known imaging apparatus that might be used in connection with the present invention, need not be specifically illustrated or discussed herein.

Computer 32 is coupled to a display 34, which is used for displaying images of slices to an operator. Included within computer 32 is a processor 36. A memory 38 (with both read only memory (ROM) and random access memory (RAM)), a storage 40 (such as a hard drive or other non-volatile data storage device) for storage of data, digital signals, and software programs, an interface 44, and a compact disk (CD) drive 46 are coupled to processor 36 through a bus 42. CD drive 46 can read a CD 48 on which machine instructions are stored for implementing the present invention and other software modules and programs that may be run by computer 32. The machine instructions are loaded into memory 38 before being executed by processor 36 to carry out the steps of the present invention.

Operation of imaging apparatus 30 is controlled by computer 32 when processor 36 executes the machine instructions stored in memory 38. These machine instructions cause the processor to implement the wall thickness estimation process discussed above, and calculation of each of the 32 morphological descriptors discussed in detail above. As lumen and outer wall boundary data are required to calculate the morphological descriptors defined above, computer 32 preferably is configured to facilitate conventional contour mapping to obtain the required lumen and outer wall boundary data. The resulting data are optionally stored on storage 40 so that selected slices can be displayed on display 34, or are directly displayed.

With respect to imaging apparatus 30, it should be understood that data from such an imaging apparatus can be collected and then stored in digital form, for later analysis by computer 32. That digital data can then later be loaded into the RAM of computer 32 via a network connection or digital memory media. Thus, imaging apparatus 30 is not required to be functionally coupled to computer 32, although such a configuration is likely to be particularly preferred, because analysis of such data can then be carried out in real-time.

Although the present invention has been described in connection with the preferred form of practicing it, those of ordinary skill in the art will understand that many modifications can be made thereto within the scope of the claims that follow. Accordingly, it is not intended that the scope of the invention in any way be limited by the above description, but instead be determined entirely by reference to the claims that follow.